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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/708,096	11.03.2000	Philip C. Wong	JHU1690-1	9634

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Lisa A Haile
Gray Cary Ware & Freidenrich LLP
4365 Executive Drive Suite 1600
San Diego, CA 92121-2189

EXAMINER

NICHOLS, CHRISTOPHER J / 0

ART UNIT PAPER NUMBER

1647

DATE MAILED: 03/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/708,096

Applicant(s)

WONG ET AL.

Examiner

Christopher Nichols, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 16 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1 and 70-75 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1 and 70-75 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on 03 November 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

1. The amendment filed 16 January 2003 (Paper No. 9) has been entered in full. Claim 1 has been amended, claims 70-75 have been added, and claims 2-69 have been cancelled. Claims 1 and 70-75 are under examination.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

3. The objections to the specification regarding the title and informalities as set forth at pp. 3 ¶ 4-6 of the previous Office Action (Paper No. 8, 11 October 2002) is *withdrawn* in view of Applicant's amendments (Paper No. 9, 16 January 2003).
4. The objection to the claims for informalities as set forth at pp. 3 ¶ 7 of the previous Office Action (Paper No. 8, 11 October 2002) is *withdrawn* in view of Applicant's amendments (Paper No. 9, 16 January 2003).
5. The rejection of claims 1, 2, 4, and 5 under 35 USC 112 ¶ 2, as set forth at pp. 7 ¶ 16 of the previous Office Action (Paper No. 8, 11 October 2002) is *withdrawn* in view of Applicant's amendments (Paper No. 9, 16 January 2003).

Maintained Objections And/Or Rejections

6. Claims 1 and 70-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

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in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons as set forth in at pp. 4-7 ¶ 8-15 of the previous Office Action (Paper No. 8, 11 October 2002). Applicant's arguments have been fully considered but are not deemed to be persuasive for the following reasons.

7. The Applicant traverses the 35 USC 112 ¶ 1 rejection of claim 1 as set forth in at pp. 4-7 ¶ 8-15 of the previous Office Action (Paper No. 8, 11 October 2002) on the grounds that the breadth of the claim has been amended to only read on an antibody that inhibits β -site APP-cleavage enzyme (BACE1, also known as β -secretase) (pp. 5-6 **D** Paper No. 9). The Applicant argues that the specification teaches a method of making an anti-BACE1 antibody (pp. 6 **D** Paper No. 9). It is noted that the Applicant has cancelled claims 2-69 and added claims 70-75 which are dependent claims of claim 1. Therefore, the rejection of claim 1 is applied to the newly added dependent claims, 70-75.

8. Via amendment, the Applicant has overcome the problem of scope (inhibition), the agent in question (antibody), and the nature of the system (*in vitro*) via amendment but not the issue of enablement. The specification teaches an *in vitro* method of measuring APP cleavage by BACE1 including controls of samples from BACE1^{-/-} transgenic mice. However, neither the specification nor the prior art teaches an antibody with anti-BACE1 activity.

9. Concerning the Applicant's assertion that the specification teaches how to make an anti-BACE1 antibody and any given anti-BACE1 antibody will have the desired anti-BACE1 activity. It is maintained that a person of ordinary skill in the art at the time of the invention would not have a reasonable expectation of success. For example, Yan et al. [(28 September 2001) "The Transmembrane Domain of the Alzheimer's β -Secretase (BACE1) Determines its

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Late Golgi Localization and Access to β -Amyloid Precursor Protein (APP) Substrate.” Journal of Biological Chemistry 276(39): 36788-36796] teaches the generation and use of anti-BACE1 antibodies, the reference does not teach the antibodies as having an inhibitory effect on BACE1 (pp. 36789; Fig. 1 and 2). In fact, Yan et al. used mutagenesis to disrupt the activity BACE1 (Fig. 6).

10. Further, Farzan et al. [(15 August 2000) “BACE2, a β -secretase homolog, cleaves at the β site and within the amyloid- β region of the amyloid- β precursor protein.” PNAS 97(17): 9712-9717 (**IDS #AB**)] teaches that the M671V mutation in APP inhibits both BACE1 and BACE2 β -site cleavage but does not teach an antibody with such activity (Fig. 5; pp. 9716).

11. Due to the large quantity of experimentation necessary to identify an antibody with anti-BACE1 activity, the lack of direction/guidance presented in the specification regarding antibody with anti-BACE1 activity, the absence of working examples directed to antibody with anti-BACE1 activity, the complex nature of the invention [Vassar (2001) “The β -Secretase, BACE” Journal of Molecular Neuroscience 17(2): 157-170, especially pp. 167-168], and the breadth of the claims which fail to recite limitations antibody with anti-BACE1 activity, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

12. Finally, the Applicant’s argument has been taken into full consideration and is not found persuasive. The Applicant has failed to show any convincing evidence in the prior art or specification of an antibody capable of inhibiting BACE1 cleavage of APP. Therefore, the rejection of claims 1 and 70-75 under 35 USC 112 ¶1 is maintained.

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Summary

13. No claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher J. Nichols whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

CJN
February 24th, 2003

Elizabeth C. Sherman